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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/846,637	04/30/2001	Michael C. Jensen	24751-2502	4845

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/846,637	JENSEN, MICHAEL C.	
	Examiner	Art Unit	
	Yong D Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73-74, 142-143, 190-191, 206-207, 219-220, 234-235, 248-249, 260-261 and 270-285* is/are pending i the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73,74,142,143,190,191,206,207,219,220,234,235,248,249,260,261 and 270-285* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on May 17, 2004, canceling claims 23-24, 27-41, 50-54, 63, 81-82, 85, 141, 143, 166-189, 192-205, 208-218, 221-233, 236-248, 250-259, 262-263, 265-266 and 268-269 and amending claims 73-74, 142-143, 190-191, 206-207, 219-220, 234-235, 248-249, 260-261 and 270-285, has been entered.

Claims 73-74, 142-143, 190-191, 206-207, 219-220, 234-235, 248-249, 260-261 and 270-285 are pending.

The finality of the rejection of the last Office action is withdrawn.

Allowable Subject Matter

The indicated allowability of claims 73-74, 142-143, 190-191, 206-207, 219-220, 234-235, 248-249, 260-261 and 270-285 are withdrawn in view of a new rejection.

Claim Objections

Claims 206-207, 270-271, 274-277 and 280-283 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 190-191. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The claims are all drawn to a method comprising human IMPDH type II protein.

Claims 248-249 and 272-273 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 234-235. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The claims are all drawn to a method comprising human IMPDH type II protein and mammalian cells.

Claims 260-261, 278-279 and 284-285 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 219-220. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The claims are all drawn to a method comprising human IMPDH type II protein and human cells

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 73-74, 142-143, 190-191, 206-207, 219-220, 234-235, 248-249, 260-261 and 270-285 are rejected under 35 U.S.C. 103(a) as being unpatentable over Farazi et al. in view of Lightfoot et al. and Roelant et al.

Farazi et al. (cited on previous form PTO-892) teach mutants of human IMPDH type II that are resistant to inhibitors of wildtype IMPDH (abstract and page 961). Farazi et al. teach that inhibitors of IMPDH have antiproliferative activity (page 961). Farazi et al. teach that MPA, MPA derivatives and mycophenolate mofetil are specific inhibitors of IMPDH (page 961). Farazi et al. teach that mutant IMPDH which are resistant to MPA can be very useful in anti-infective chemotherapy (page 961).

Wildtype human IMPDH II and DNA encoding the enzyme is well known in the art (Collart et al. – form PTO-1449). Wildtype IMPDH and the mutant IMPDH of the instant invention, SEQ ID NO:4, is different at residues 190, 191, 333 and 351. However, Farazi et al. teaches that the wildtype sequenced by Collart et al. was incorrect, and that wild type human IMPDH II naturally has an alanine at residue 190 and Glycine at residue 191 (page 962, third full paragraph). Therefore, the only difference between the mutant of the instant invention and wild type IMPDH II is at residues 333 and 351.

However, Lightfoot et al. (form PTO-1449) teaches a mutant mouse IMPDH having resistance to MPA (abstract). The mutant IMPDH of Lightfoot et al. has two point mutations, Thr-333-Ile and Ser-351-Tyr (abstract). Human wild type IMPDH type II also has a Thr at residue 333 and Ser at residue 351. The two mammalian enzymes are also highly homologous.

In the state of the art, there are many methods thought which one can ascertain the result of a mutagenized enzyme. One way is to perform cell proliferation assays since inhibitors of IMPDH have antiproliferative activity where resistance against the inhibitors of IMPDH corresponds to an increase in the proliferation of the cells containing the mutant IMPDH.

Cell proliferation assays are well known in the art. Roelant et al. (U.S. Patent No. 5,306,624) teach how to perform proliferation assay by quantifying the number of viable cells (abstract and claims). Stratagene is one of many companies that teach how to perform cell proliferation assays (from PTO-892). cited previously

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make two mutations with human IMPDH type II and screen whether the mutants have resistance against inhibitors of IMPDH by performing cell proliferation assays, quantifying viable cells containing the mutant enzymes and cell containing wildtype IMPDH. The motivation of applying the teachings of Lightfoot et al. to human IMPDH is for potential use of the mutant enzyme in human, such as for anti-infective chemotherapy. Also, the mutant can be used for designing IMPDH inhibitors that are species-selective. The motivation of performing the cell proliferation assay is to determine if the mutant IMPDH are resistant to IMPDH inhibitors since inhibition of IMPDH results in anti-proliferative activity. One of ordinary skill in the art would have had a reasonable expectation of success since Longfoot et al. teaches a mutant IMPDH that is resistant to MPA while retaining enzymatic activity.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner

PONNATHAPU ACHUTAMURTHY
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